

Poloxamer

1 Nonproprietary Names

BP: Poloxamers
PhEur: Poloxamera
USPNF: Poloxamer

2 Synonyms

Lutrol; *Monolan*; *Pluronic*; poloxalkol; polyethylene-propylene glycol copolymer; polyoxyethylene-polyoxypropylene copolymer; *Supronic*; *Synperonic*.

3 Chemical Name and CAS Registry Number

α -Hydro- ω -hydroxypoly(oxyethylene)poly(oxypropylene) poly(oxyethylene) block copolymer [9003-11-6]

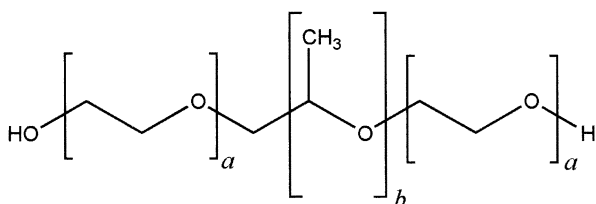
4 Empirical Formula Molecular Weight

The poloxamer polyols are a series of closely related block copolymers of ethylene oxide and propylene oxide conforming to the general formula $\text{HO}(\text{C}_2\text{H}_4\text{O})_a(\text{C}_3\text{H}_6\text{O})_b(\text{C}_2\text{H}_4\text{O})_a\text{H}$. The grades included in the PhEur 2002 and USPNF 20 are shown in Table I. The PhEur 2002 states that a suitable antioxidant may be added.

Table I: Typical poloxamer grades.

Poloxamer	Physical form	a	b	Average molecular weight
124	Liquid	12	20	2 090–2 360
188	Solid	80	27	7 680–9 510
237	Solid	64	37	6 840–8 830
338	Solid	141	44	12 700–17 400
407	Solid	101	56	9 840–14 600

5 Structural Formula



6 Functional Category

Dispersing agent; emulsifying and coemulsifying agent; solubilizing agent; tablet lubricant; wetting agent.

7 Applications in Pharmaceutical Formulation or Technology

Poloxamers are nonionic polyoxyethylene-polyoxypropylene copolymers used primarily in pharmaceutical formulations as

emulsifying or solubilizing agents.^(1–8) The polyoxyethylene segment is hydrophilic while the polyoxypropylene segment is hydrophobic. All of the poloxamers are chemically similar in composition, differing only in the relative amounts of propylene and ethylene oxides added during manufacture. Their physical and surface-active properties vary over a wide range and a number of different types are commercially available; see Sections 4, 9, 10, and 18.

Poloxamers are used as emulsifying agents in intravenous fat emulsions, and as solubilizing and stabilizing agents to maintain the clarity of elixirs and syrups. Poloxamers may also be used as wetting agents; in ointments, suppository bases, and gels; and as tablet binders and coatings.

Poloxamer 188 has also been used as an emulsifying agent for fluorocarbons used as artificial blood substitutes and in the preparation of solid-dispersion systems.

More recently, poloxamers have found use in drug-delivery systems.^(9–14)

Therapeutically, poloxamer 188 is administered orally as a wetting agent and stool lubricant in the treatment of constipation; it is usually used in combination with a laxative such as danthron. Poloxamers may also be used therapeutically as wetting agents in eye-drop formulations, in the treatment of kidney stones, and as skin-wound cleansers.

Poloxamer 338 and 407 are used in solutions for contact lens care. See Table II.

Table II: Uses of poloxamer.

Use	Concentration (%)
Fat emulsifier	0.3
Flavor solubilizer	0.3
Fluorocarbon emulsifier	2.5
Gelling agent	15–50
Spreading agent	1
Stabilizing agent	1–5
Suppository base	4–6 or 90
Tablet coating	10
Tablet excipient	5–10
Wetting agent	0.01–5

8 Description

Poloxamers generally occur as white, waxy, free-flowing prilled granules, or as cast solids. They are practically odorless and tasteless. At room temperature, poloxamer 124 occurs as a colorless liquid.

9 Pharmacopeial Specifications

See Table III.

10 Typical Properties

Acidity/alkalinity: pH = 5.0–7.4 for a 2.5% w/v aqueous solution.

Cloud point: >100°C for a 1% w/v aqueous solution, and a 10% w/v aqueous solution of poloxamer 188.

Table III: Pharmacopeial specifications for poloxamer.

Test	PhEur 2002 (Suppl 4.3)	USPNF 20
Identification	+	—
Characters	+	—
Appearance of solution	+	—
Melting point	≈ 50°C	—
Average molecular weight		
For poloxamer 124	2 090–2 360	2 090–2 360
For poloxamer 188	7 680–9 510	7 680–9 510
For poloxamer 237	6 840–8 830	6 840–8 830
For poloxamer 338	12 700–17 400	12 700–17 400
For poloxamer 407	9 840–14 600	9 840–14 600
Weight percent oxyethylene		
For poloxamer 124	44.8–48.6	46.7 ± 1.9
For poloxamer 188	79.9–83.7	81.8 ± 1.9
For poloxamer 237	70.5–74.3	72.4 ± 1.9
For poloxamer 338	81.4–84.9	83.1 ± 1.7
For poloxamer 407	71.5–74.9	73.2 ± 1.7
pH (aqueous solution)	5.0–7.5	5.0–7.5
Unsaturation (mEq/g)		
For poloxamer 124	—	0.020 ± 0.008
For poloxamer 188	—	0.026 ± 0.008
For poloxamer 237	—	0.034 ± 0.008
For poloxamer 338	—	0.031 ± 0.008
For poloxamer 407	—	0.048 ± 0.017
Oxypropylene:oxyethylene ratio+		—
Total ash	≤ 0.4%	—
Heavy metals	—	≤ 0.002%
Organic volatile impurities	—	+
Water	≤ 1.0%	—
Free ethylene oxide, propylene + oxide and 1,4-dioxane		≤ 5 ppm

Density: 1.06 g/cm³ at 25°C

Flash point: 260°C

Flowability: solid poloxamers are free flowing.

HLB value: 0.5–30; 29 for poloxamer 188.

Melting point:

16°C for poloxamer 124

52–57°C for poloxamer 188

49°C for poloxamer 237

57°C for poloxamer 338

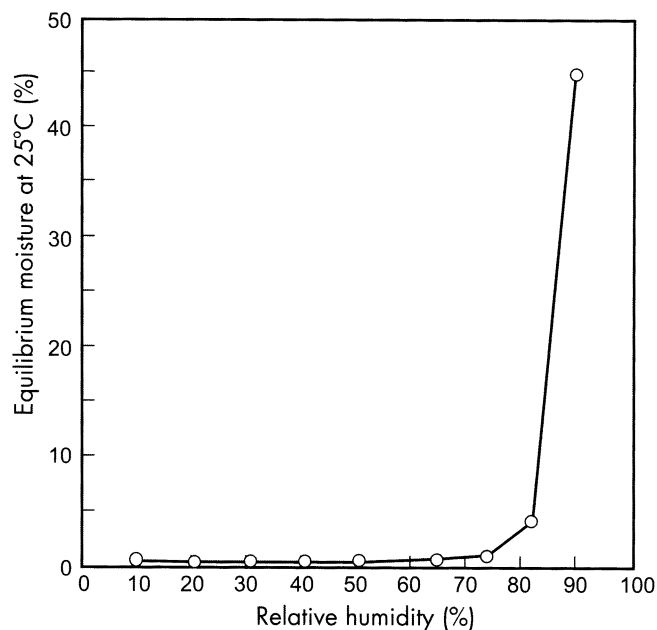
52–57°C for poloxamer 407

Moisture content: poloxamers generally contain less than 0.5% w/w water and are hygroscopic only at relative humidity greater than 80%. See also Figure 1.

Solubility: solubility varies according to the poloxamer type; see also Table IV.

Table IV: Solubility at 20°C for various types of poloxamer in different solvents.

Type	Solvent				
	Ethanol (95%)	Propan-2-ol	Propylene glycol	Water	Xylene
Poloxamer 124	Freely soluble	Freely soluble	Freely soluble	Freely soluble	Freely soluble
Poloxamer 188	Freely soluble	—	—	Freely soluble	—
Poloxamer 237	Freely soluble	Sparingly soluble	—	Freely soluble	Sparingly soluble
Poloxamer 338	Freely soluble	—	Sparingly soluble	Freely soluble	—
Poloxamer 407	Freely soluble	Freely soluble	—	Freely soluble	—

**Figure 1:** Equilibrium moisture content of poloxamer 188 (Pluronic F-68).

Surface tension:

19.8 mN/m (19.8 dynes/cm) for a 0.1% w/v aqueous poloxamer 188 solution at 25°C

24.0 mN/m (24.0 dynes/cm) for a 0.01% w/v aqueous poloxamer 188 solution at 25°C

26.0 mN/m (26.0 dynes/cm) for a 0.001% w/v aqueous poloxamer solution at 25°C

Viscosity (dynamic): 1000 mPa s (1000 cP) as a melt at 77°C for poloxamer 188.

11 Stability and Storage Conditions

Poloxamers are stable materials. Aqueous solutions are stable in the presence of acids, alkalis, and metal ions. However, aqueous solutions support mold growth.

The bulk material should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

Depending on the relative concentrations, poloxamer 188 is incompatible with phenols and parabens.

13 Method of Manufacture

Poloxamer polymers are prepared by reacting propylene oxide with propylene glycol to form polyoxypropylene glycol. Ethylene oxide is then added to form the block copolymer.

14 Safety

Poloxamers are used in a variety of oral, parenteral, and topical pharmaceutical formulations and are generally regarded as nontoxic and nonirritant materials. Poloxamers are not metabolized in the body.

Animal toxicity studies, with dogs and rabbits, have shown poloxamers to be nonirritating and nonsensitizing when applied in 5% w/v and 10% w/v concentration to the eyes, gums, and skin.

In a 14-day study of intravenous administration at concentrations up to 0.5 g/kg/day to rabbits, no overt adverse effects were noted. A similar study with dogs also showed no adverse effects at dosage levels up to 0.5 g/kg/day. In a longer-term study, rats fed 3% w/w or 5% w/w of poloxamer in food for up to 2 years did not exhibit any significant symptoms of toxicity. However, rats receiving 7.5% w/w of poloxamer in their diet showed some decrease in growth rate.

No hemolysis of human blood cells was observed over 18 hours at 25°C, with 0.001–10% w/v poloxamer solutions.

Acute animal toxicity data for poloxamer 188:⁽¹⁵⁾

- LD₅₀ (mouse, IV): 1 g/kg
- LD₅₀ (mouse, oral): 15 g/kg
- LD₅₀ (mouse, SC): 5.5 g/kg
- LD₅₀ (rat, IV): 7.5 g/kg
- LD₅₀ (rat, oral): 9.4 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and gloves are recommended.

16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (IV injections; inhalations, ophthalmic preparations; oral powders, solutions, suspensions, and syrups; topical preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

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18 Comments

Although the USPNF 20 contains specifications for five poloxamer grades, many more different poloxamers are commercially available that vary in their molecular weight and the proportion of oxyethylene present in the polymer. A series of poloxamers with greatly varying physical properties are thus available.

The nonproprietary name 'poloxamer' is followed by a number, the first two digits of which, when multiplied by 100, correspond to the approximate average molecular weight of the polyoxypropylene portion of the copolymer and the third digit, when multiplied by 10, corresponds to the percentage by weight of the polyoxyethylene portion.

Similarly, with many of the trade names used for poloxamers, e.g., *Pluronic F-68* (BASF Corp), the first digit arbitrarily represents the molecular weight of the polyoxypropylene portion and the second digit represents the weight percent of the oxyethylene portion. The letters 'L', 'P', and 'F', stand for the physical form of the poloxamer: liquid, paste, or flakes; see also Table V.

Table V: Nonproprietary name and corresponding commercial grade.

Nonproprietary name	Commercial grade
Poloxamer 124	L-44
Poloxamer 188	F-68
Poloxamer 237	F-87
Poloxamer 338	F-108
Poloxamer 407	F-127

Note that in the USA the trade name *Pluronic* is used by BASF Corp. for pharmaceutical-grade and industrial-grade poloxamers, while in Europe the trade name *Lutrol* is used by BASF Corp. for the pharmaceutical-grade material.

Poloxamers for use in the cosmetic industry as oil-in-water emulsifiers, cleansers for mild facial products, and dispersing agents are marketed by BASF Corp. as *Pluracare*. The grades available are listed in Table VI.

Table VI: Nonproprietary name and corresponding *Pluracare* grade (BASF Corp.).

Nonproprietary name	Commercial grade	HLB value	pH of 2.5% w/v aqueous solution
Poloxamer 184	L-64	12–18	5–7.5
Poloxamer 185	P-65	12–18	6–7.4
Poloxamer 407	F-127	18–23	6–7.4

19 Specific References

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20 General References

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21 Author

JH Collett.

22 Date of Revision

6 November 2002.